A White Paper from the Endocrine Society
December 2007

Increasing Minority Participation in Clinical Research

ENDOCRINE SOCIETY

The Endocrine Society's Task Force on Increasing Minority Participation in Clinical Research

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Supported by a grant from the Robert Wood Johnson Foundation

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INTRODUCTION

Maria Alexander-Bridges, M.D. Ph.D., and Loretta L. Doan, Ph.D.

Primary Goal

Our goal is to ensure that clinical research supporting 1) the safety and efficacy of products for labeling purposes and 2) the validity of biomarkers commonly used to assess risk and to design therapeutic strategies is based on data sufficient for statistical power and derived from diverse subpopulations.

It is widely recognized that data supporting therapeutic options for women and minorities have been deficient because these groups were not previously included in clinical trials. Although the combined efforts of Congress, the Office of Women's Health at the Food and Drug Administration (FDA), and the Office of Research on Women's Health at the National Institutes of Health (NIH) have been quite successful in reversing the shortage of data to support therapeutic options for women, the problem of obtaining data with adequate statistical power across race, ethnicity, and socioeconomic groups has yet to be broadly addressed.

In the academic setting, where NIH and certain independent research foundations have targeted funding to ensure minority participation in large, multi-center trials, investigators have attained and even surpassed their recruitment goals. In the process, thoughtful communications strategies and best practices for surmounting common impediments to minority participation have evolved. Unfortunately, sufficient funds for the public relations efforts required to ensure inclusion are not uniformly available to individual investigators as they undertake each new trial. This makes it important to identify and remove the infrastructural barriers that impede participation of diverse volunteers in trials led by academic and commercial entities.

Our work has led us to conclude that the consistent recruitment of large numbers of minority and economically disadvantaged research volunteers will require new initiatives. In particular, we think it will be important to facilitate collaboration between the diverse group of community-based physicians who serve underrepresented populations and the physician-scientists who have traditionally performed clinical trials on behalf of academic and pharmaceutical entities. We base this conclusion on research that reviewed the decision-making process of 70,000 research volunteers and showed that minority volunteers are just as likely as majority volunteers to participate in clinical trials *when approached by their own physicians*. Restated, this study dispelled the prevailing myth that minority volunteers fail to participate in trials because they harbor distrust of research and researchers; instead the limiting factor appears to be whether minority patients are asked to participate. Further, inasmuch as minority patients often choose physicians from their own racial and ethnic background, lack of access to clinical trials for the minority physician would translate into lack of access for the minority patient.

The insight that access might be the limiting factor determining participation rates has led Ken Getz and Alfonso Alanis, two members of the Society's task force, to assess the degree to which minority physicians themselves have access to, and participate in, clinical trials. This is an important question because of the essential difference between the recruitment methods of academic investigators—who recruit individual patients—and those of investigators at pharmaceutical companies/contract research organizations (CROs) who recruit research "sites" consisting of one or more physicians and their patients. The critical tactic in the pharmaceutical setting, where new therapeutics are being developed, is to ensure that minority physicians in practice are being asked to participate in industry-sponsored trials by either the sponsoring pharmaceutical companies or the CROs that assist in recruiting research sites. Accordingly, we conclude that pharmaceutical companies and CROs will have more success recruiting diverse populations to their clinical trials if they first attack the infrastructural impediments, namely the lack of diverse physicians in their pool of investigators. Once clinical sites that serve diverse patients are identified, it will also be easier to undertake appropriate education efforts on behalf of patients at these sites and start to address the barriers that discourage individual volunteers from participating in trials performed at these sites when asked to do so.

Further, we suggest that academic institutions would do well to study and possibly adopt the mechanisms used by pharmaceutical companies to recruit patients. For example, developing contract research organizations that specialize in providing ready access to diverse sites may, in the long term, benefit academic institutions doing NIH-funded research as well as corporate entities. Such an approach would reduce the need to implement expensive and time-consuming

efforts to diversify each new NIH trial. We therefore suggest all agencies that fund/implement clinical research—NIH, foundations, pharmaceutical companies, and medical centers—would benefit from working together to build a network of diverse, community-based practitioners who can participate in clinical trials. This would require work on the *pipeline* to increase the number of diverse students, fellows, and faculty willing to become clinical investigators, as well as outreach to the community to *identify diverse practitioners who would be willing to receive training* in the implementation of good clinical research practices.

Over the long term, there is little doubt that the nationwide effort required to attain the aforementioned goals will occur. The emerging field of pharmacogenomics will provide insight into the genetic differences that underlie disparate responses to therapeutic agents in individual patients. As we gain a better understanding of the genetic variations that affect specific disease genes and the metabolism of therapeutic compounds, the differences that distinguish racial groups will become clearer. It is possible that the need for statistically powerful clinical trials on distinct subpopulations may diminish with time. However, in the near future, easy access to minority populations will be essential to validate hypotheses derived from these pharmacogenomic studies. The full benefits of pharmacogenomics will only be evident in the distant future, and until then we have a responsibility to ensure the safety and efficacy of current products, and products in development, for all our citizens. We therefore conclude that increasing minority subpopulation inclusion in clinical research must remain a primary goal in the immediate future. As forward-looking pharmaceutical companies incorporate "personalized medicine" or "mass personalization" of medicine into their strategies for drug development and validation, CROs that can provide diverse clinical sites will command a significant competitive advantage. As the viability of CROs begins to depend on their ability to provide diverse sites, they will find the resources to do so.

We understand that significant change in our way of organizing clinical trials will only come at great expense and with consistent effort over several years. Creating change will require interventions at multiple levels that no company or agency could be expected to undertake alone. Consequently, we recommend that NIH, FDA, or an independent group organize a forum in which government agencies, pharmaceutical companies, academia, and patient interest groups convene to think through the objectives, expectations, and structure for overseeing the implementation of infrastructural changes needed to support the inclusion of broad patient bases in clinical research efforts. Only with such a process will it be possible for all the diverse subpopulations in these United States to benefit from current and future advances.

In the meantime, we believe that Congress and regulatory agencies such as the FDA will need to increase their efforts to ensure that new product labeling is supported by safety and efficacy studies that include all relevant subpopulations.

In the final section of this white paper (beginning on page 26), we outline the Society's full set of detailed recommendations—both short- and long-term—for attaining these goals. We briefly summarize only a subset of those recommendations here:

All stakeholder groups should:

- Participate in a series of summits to establish firm priorities, procedures, and timelines.

Congress should:

- Pass legislation requiring inclusion of minorities in clinical trials for FDA approval of drugs.
- Establish and/or empower an Office of Minority Health within the FDA.

FDA should:

- Adopt NIH guidelines on the inclusion of women and minority populations.
- Require rather than recommend adherence to its guidelines.

NIH and academic institutions should:

- Establish and maintain an infrastructure of minority physician and patient volunteers.
- Establish training and/or mentorship programs for community-based physicians.
- Provide annual training in Good Clinical Research Practices and Cultural Competencies.

Each stakeholder group approaches the problem from its own perspective, and these different views are represented independently in the four sections immediately following this introduction. Because each viewpoint is unique, so are the recommendations and best practices presented in each of the four sections. The recommendations presented in the final section were reached by consensus among all members of the writing group and represent The Endocrine Society's official recommendations for addressing the problem at hand.

Minority Participation in Clinical Trials: An Elusive Goal

Perspectives from the Pharmaceutical Companies and Contract Research Organizations' Point of View

Alfonso J. Alanis, M.D.† and Ken Getz, M.S., M.B.A.‡

Representation of Ethnic Minorities in Clinical Trials

- **For many years, ethnic minorities have been and continue to be significantly under-represented in clinical trials and little has been done to change this.**

  Health care inequalities that disproportionately affect ethnic minority groups have been recognized for many decades. Congruently, the under-representation of ethnic minority groups in clinical research has been, and continues to be, a major component of health care deficiencies in the United States. The under-representation of minorities occurs in all types of clinical research and all therapeutic areas, including those diseases that predominantly affect ethnic minorities. Regrettably, little progress has been made toward including minorities in clinical research and the key parties involved in planning and conducting clinical trials (investigators, sponsors, and regulators), have not yet given full priority to inclusion.

  Upon directives in legislation passed by Congress in the early 1990s, the National Institutes of Health (NIH) instituted policies aimed at increasing the representation of minority populations in clinical trials funded by the agency. NIH's policy and guidelines are described in a separate section of this document and are a good example of how change can be implemented.

- **The United States' minority populations, who carry an increased burden of disease, will be the majority in 2050.**

  According to the most recent update to the 2000 U.S. Census via the "2005 American Community Survey," ethnic minorities comprise 37.5% of the general population of the United States, and Hispanics have become the largest ethnic minority group, accounting for 14.5% of the general population followed by African Americans at 12.1%, Asians at 4.3%, and Native Americans at 0.9% of the population.

  In addition, projections of new births and immigration predict that as an aggregate, ethnic minority groups will make up 51% of the entire U.S. population by 2050. Hispanics and Asian groups, in particular, will double their representation in the general population between 2000 and 2050.

- **Under-representation of minorities in clinical research means treated populations may have been under-studied or never studied.**

  When clinical trial data are generated on diseases that particularly affect minority populations, the data are not necessarily applicable to all the key ethnic minorities who suffer a higher burden of these diseases if these minorities have been under-represented or not included in the studies. In many instances, diagnostic and therapeutic decisions that affect patients' well-being and health outcomes are based on data gathered in populations of patients not representative of the patients who will bear the consequences of these decisions.

- **Many barriers to the participation of minorities in clinical trials have been studied and recognized in the past.**

  Many studies have tried to understand the reasons that minorities are under-represented in clinical studies and there appear to be multiple barriers to participation. The most important relates to the fact that some minorities may have greater distrust of the medical system. This lack of trust is particularly important for African American patients and is rooted in the legacy of the Tuskegee Syphilis studies conducted by the U.S. Public Health Service from 1932 to 1972. In those studies, nearly 400 patients with syphilis were deprived of appropriate therapy and were simply "observed" over a period of nearly 40 years to "better understand the natural history of the disease." Lack of trust is also an issue with Hispanic patients who remember the oral contraceptive studies done with Hispanic women in the 1960s. Researchers did not provide patients with

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Table I: Consent Rate by Ethnicity/Race in More Than 90,000 Patients Offered Enrollment in 20 Studies[1]

	Non-Hispanic White		African-American		Hispanic		All Minorities	
Type of Study Analyzed	Offered Enrollment	Consent Rate	Offered Enrollment	Consent Rate	Offered Enrollment	Consent Rate	Offered Enrollment	Consent Rate
Interviews and Non-Intervention (3)	46,713	83.5%	12,614	82.2%	14,497	86.1%	27,111	84.3%
Clinical Intervention Trials (10)	6,724	41.8%	1,604	45.3%	555	55.9%	2,159	48.0%
Surgical Intervention Trials (7)	7,756	47.8%	NA	NA	NA	NA	398	65.8%
Subtotal:			14,218		15,052			
TOTAL:	61,193	74.4%					29,668	81.4%

[1] **Modified from Wendler D, Kington R, Madans J, et al (2006): Are racial and ethnic minorities less willing to participate in health research? PLoS Med 3(2) e19: 201-210.**

That minorities are willing to participate in biomedical studies is contrary to "common wisdom" and "general knowledge" in medical research. The Wendler study is important because it demonstrates that despite multiple recognized and legitimate obstacles to participation in clinical studies, minority people are indeed willing to participate in clinical studies when they are offered honest information and enrollment.

appropriate information about the study, nor did they obtain informed consent.

Other recognized barriers can be cultural or religious in nature or can be related to the patient's inability to communicate in English. Studies with non–English-speaking participants require all patient documents related to study be translated; in many cases this may require "live" translation during the medical visits.

Finally, there are social and economic barriers such as the need for transportation, the need for child care during the visits, or the inability or fear of many patients regarding the loss of wages due to their participation in the clinical study. Different communities weigh these barriers differently. The barriers can be overcome, however, if the researchers are knowledgeable and display tact and cultural sensitivity.

- **Lack of access, rather than unwillingness to participate, seems to be the primary barrier to minority participation.**

  Ethnic minorities are not being invited to participate in clinical trials even when the diseases being studied predominantly affect the minority population. And, it is true that many other barriers play a role in the final decision of minority patients to participate in studies. The problem, however, is not willingness on the part of minorities. In fact some recent studies have found that minority patients are just as willing to participate in biomedical research studies as the majority population. Twenty published articles on the consent rate by race or ethnicity, and involving more than 90,000 patients, were examined by investigators from the NIH in collaboration with the CDC, Yale University, and Emory University (Wendler et al. 2006). Eighteen of these studies were conducted exclusively or predominately in the United States (n = ~89,000 patients), and two AIDS trials were conducted in Europe, Australia, and New Zealand (n = 447 patients).

  Included in this analysis were 3 non-interventional studies (simple interview or questionnaire), 10 clinical interventional studies, and 7 surgical intervention trials (Table I). In the interventional studies, African American and Hispanic patients were consistently as willing—if not even more so—as non-Hispanic white patients to participate in biomedical studies. In fact, for non-interventional and clinical interventional trials, African Americans were as willing as non-Hispanic whites to consent for participation, and Hispanics

exhibited a statistically significantly higher consent rate than the other two subgroups.

- **In summary, members of minority populations will participate when invited and will stay engaged in studies when the barriers to their participation are appropriately addressed.**

  Therefore, the appropriate participation of ethnic minorities in biomedical research studies is quite possible and is, first and foremost, an issue of access, whereas all other well-recognized and legitimate barriers remain secondary obstacles that must be managed in the design and implementation of clinical studies. Achieving optimal participation and enrollment first requires acknowledgment of the barriers, and second, requires managing the obstacles that many minorities face while trying to decide whether to participate in clinical trials.

  Unfortunately all the evidence indicates that minorities are not being given access to these studies. It appears that simply citing the well-recognized barriers to minority participation in clinical research studies has become a "reasonable and acceptable" way for investigators, sponsors, and regulators to rationalize and justify the lack of minority inclusion in biomedical research studies.

Disparities in Participation by Investigators and their Impact on Participation by Minority Volunteers

- **Minority patients are more likely to participate in clinical trials if asked by their own physicians.**

  A recent study from the Tuskegee Legacy Project assessed the likelihood of ethnic minority patients to participate in clinical research. In addition to confirming that ethnic minority candidates are willing to participate in clinical trials, they also found that patients are more likely to participate if their own primary or specialty physicians have asked them to consider participation.

- **Minority physicians often return to their communities; minority patients in those communities are more likely to choose physicians of their own ethnicity.**

  Studies have shown that minority physicians are three to four times more likely to practice in areas where they can serve members of their own ethnic group and that patients consistently choose physicians of their own ethnicity. This is especially true of primary care physicians and internists who handle the essential health care needs of communities.

- **Unfortunately, minority investigators are very poorly represented in clinical trials in the United States today.**

  Two major factors appear to influence the participation of minority practitioners as investigators in biomedical research studies: first, a limited pipeline and second, a lack of access for those minority physicians who are in practice and are interested in participating in clinical research.

  According to the Association of American Medical Colleges, African Americans, Hispanics/Latinos, and Native Americans *combined* make up only 6.4% of all physicians graduating from allopathic medical schools in the last few years, whereas Asians alone represent 5.7%. This is in spite of significant efforts by the academic community to attract larger numbers of qualified minority students to apply to medical school.

  Very little data exist regarding the participation of established minority physicians as investigators in clinical trials. However, in one never-published, small survey of clinical investigators done by the National Medical Association several years ago (Powell, J; personal communication), it was found that African American and Hispanic investigators constituted about 5% of the total pool of investigators despite the fact that these two ethnic groups represented more than 25% of the general population at the time.

  Established practicing physicians, even when well trained, experience two major impediments to participating in clinical research. First, clinical research requires an infrastructure including, among other things, staff support such as research coordinators, as well as special equipment and additional refrigerated storage space. If these investigators are not provided opportunity to regularly participate in clinical trials, they can ill afford to build and maintain the required infrastructure in their practices. Due to their tight timetables, pharmaceutical companies and CROs only recruit physicians with a track record of clinical research. Therefore, physicians with an interest in clinical research, but with little experience, lack the opportunities to participate in enough clinical trials to maintain the infrastructure that they have worked so hard to build.

This results in minority physicians being under-represented in clinical research and, as a consequence, their patients, many of whom belong to ethnic minority groups, are also under-represented.

- **Minority physicians who have access to minority patients can be an important source of ethnic minority volunteers for clinical trials**.

  As stated above, minority physicians practicing in the communities and neighborhoods where ethnic minorities live rapidly gain the trust of these communities and easily "bond" with their patients, who tend to trust their doctors and will likely follow their advice. If these practicing physicians, who are beyond their formal training period, were instructed in the Principles of Clinical Research and Good Clinical Practice, they could become well-qualified investigators and an important source of ethnic minority patients for clinical trials.

The Role of the Pharmaceutical Industry and Contract Research Organizations (CROs) in the Inclusion of Ethnic Minorities in Clinical Trials

- **The vast majority of clinical trials testing novel therapies for medical illnesses are sponsored by pharmaceutical, biotechnology, and medical-device companies.**

  Clinical trials can be sponsored by different types of institutions (individual doctors, medical institutions, universities, foundations, voluntary groups, NGOs, insurance companies, or federal agencies such as the National Institutes of Health). However, most of the clinical trials aimed at researching new medical treatments are sponsored by the pharmaceutical, the biotechnology, or the medical-devices industries. Academic institutions and federal agencies comprise the other large group of institutions that sponsor such studies.

  It is important to note that academic institutions and pharmaceutical companies recruit patients in different ways. Academic institutions with clinical researchers on faculty recruit individual patients into individual trials. In contrast, the pharmaceutical industry relies on the recruitment of research sites, which means that physicians in practice are recruited to participate in a research protocol and these physicians recruit patients from their own patient base to participate in the trial. Companies often, but not always, enlist a Contract Research Organization (CRO) to oversee the recruitment and activities of clinical study sites. In some cases the CRO will help identify sites. In order to create change in minority participation in academia the investigator leading the trial must increase efforts to identify and recruit minority patients. At the level of the pharmaceutical company, where most of the trials that lead to drug approval are done, efforts must be made to recruit diverse research "sites," that is, diverse physician practices that serve diverse patients. Inasmuch as diverse patients seek physicians from a similar background, it will be necessary to identify and recruit sites run by minority physicians and/or physicians in diverse communities to increase participation of minority volunteers in clinical trials.

- **The limited patent life of new products and the long development cycle time puts pressure on pharmaceutical companies to deliver their new products as soon as possible.**

  The key priority for pharmaceutical companies is to develop their new products as fast as they can while focusing on the quality of the data generated in their clinical trials. The financial pressure to meet the speed and quality objectives of pharmaceutical companies has left little time for CROs to focus on anything else, including the appropriate inclusion of ethnic minority patients into their clinical research studies.

- **The inclusion of ethnic minorities as clinical trial participants adds complexity and cost.**

  The added complexity of recruiting minority physicians and volunteers has traditionally translated into time delays for the entire project and this added cost increases an already large investment. There is no question, however, that the experienced investigator can plan ahead, accommodate these additional needs, and manage them effectively.

  Although anecdotal accounts suggest that overruns for enrolling minorities can be 20% to 30% of the total study budget, this is not typically the case. These costs can add up to 10% or 15% of the total budget, however, when there are needs for such extras as translation services, transportation to and from the investigator's office, payment for nursing care, or restitution of lost wages.

In summary, to successfully enroll and retain ethnic minority patients in clinical trials, there is a need not only for additional effort on the part of the investigators but also for additions to the budget. In many cases, adding these elements to an existing clinical plan can be perceived as potentially delaying full enrollment of the study and ultimate approval of a new drug. Taken together, these issues lead us to believe that it is important to change the infrastructure to focus on developing a clinical research base of physicians who serve urban areas who will be ready and willing to participate in clinical trials.

- **There is no clear-cut regulatory mandate for inclusion.**

  As of today, May 2007, the United States Food and Drug Administration (FDA) has chosen not to make it mandatory for pharmaceutical, biotechnology, and medical-device companies to include ethnic minorities in their registration or pharmacovigilance clinical trials. In fact, the only guidance from the FDA is titled "Collection of Race and Ethnicity Data in Clinical Trials" and it focuses on the logistics of reporting race and ethnicity data in clinical trials and not on the appropriate inclusion of minorities.

- **Site recruitment has been a matter of convenience.**

  In the rush to recruit investigative sites for their clinical trials, pharmaceutical companies turn to the most convenient and accessible methods to identify candidates. Minority-based investigative sites have not been well represented in the internal and commercial resources (e.g., directories and databases) used by pharmaceutical companies during the site-selection process.

- **Why have CROs not addressed this issue?**

  CROs oversee the conduct of clinical trials and as such might be expected to indicate when minority inclusion is especially important. However, CROs cater their services to the demands of their customers and they try to focus on meeting the needs and expectations of these customers—the pharmaceutical, biotechnology, and medical-device companies. As a result, "traditional" CROs have not developed the expertise to include ethnic minorities in clinical research and they are unlikely to do this any time soon. After all, as with the pharmaceutical companies, their focus has been and continues to be on the speed and quality of clinical trial implementation.

  Unless mandated by the regulatory authorities, CROs are even less likely than pharmaceutical companies to make changes in this area. CROs do not regard including ethnic minorities in clinical research as an inherently high priority. Even if eventually forced to do so, many CROs will find it a struggle to achieve minority inclusion because they do not understand the associated complexities and costs, nor have they cultivated the relationships needed to gain access to ethnic minority patients and physicians.

- **What is the likelihood that the requirements for inclusion will change?**

  That inclusion of diverse subpopulations is essential is very likely to become evident, as we continue to gain a better understanding of how drugs are managed differently by different body systems, resulting in differences in the efficacy and the safety profiles of these drugs in different subpopulations.

  The concept of differences in response among ethnic groups is relatively new. In the 1980s, it was discovered that ethanol is metabolized differently in about 50% of Asian patients due to the presence of an inactive variant of an enzyme that metabolizes alcohol. When they consume alcohol, individuals with the inactive enzyme experience a "dysphoric reaction" characterized by flushing of the facial skin, tachycardia, and increased skin temperature. This unpleasant reaction has been cited as a reason for the lower incidence of alcohol abuse in the population expressing the variant enzyme. More recently, this same enzyme has been found also to help activate nitroglycerin, which is commonly used to treat heart-attack patients. The same inactive enzyme, then, would decrease the efficacy of nitroglycerin treatment. This means that about 50% of Asian patients treated with this drug might not respond to it during an acute coronary attack.

  Similarly, aspirin has been found to have different protective effects in men and women. More recently, a new drug developed for the treatment of lung cancer, Iressa, was found to induce pulmonary fibrosis at a higher rate in Japanese patients than in non-Japanese Americans (2% vs. 0.3%).

  Two years ago, the FDA broke new ground by approving the first drug with race-specific indications.

The cardiovascular drug BiDil® combines two well known vasodilating cardiovascular drugs (isosorbide dinitrate and hydralazine hydrochloride) for the treatment of advanced congestive heart failure specifically in black patients. The approval results from findings that although the combination confers benefits to black patients, it has not been particularly beneficial for the treatment of the same condition in other ethnic groups.

It is clear from these recent advances that the medical community is learning to recognize different levels of efficacy and safety of drugs in different ethnic groups.

- **Recent advances notwithstanding, the FDA does a poor job of requiring and classifying race information in clinical trials.**

  The FDA does not require inclusion of representative minority populations in clinical trials and has even failed to enforce and implement its own existing regulations. Current regulations merely make it mandatory to report the ethnicity of patients in all clinical trials submitted for registration approval of new medical treatments. As a result of poor regulations and even poorer enforcement, nearly half of all trials accepted for review by the FDA today do not contain any information on the ethnicity of the patients studied.

  In the new age of medicine we seek to "personalize" the development of new treatments so that new therapies can be targeted to "the right patient at the right time," thus maximizing efficacy while minimizing toxicity. For this goal to be realized, it will be even more critical to collect data on the responses of all racial and ethnic groups to new drugs. This is a conclusion that is slowly being reached by the medical community.

  It appears that pharmaceutical companies, regulators, and many academic institutions are increasingly recognizing that it makes little sense to conduct a clinical research study among patients who are different from those who will actually be treated with the technologies they seek to develop. Scientifically, it makes no sense to develop new treatments among populations of patients who are different from those who will be using them. If the future of clinical research is to include enhancing the scientific value of the observations made, investigators will need to include members of racial and ethnic minorities while developing new treatments for diseases that disproportionately affect those groups.

Recommendations from the Pharmaceutical Company/CRO Perspective

- Those responsible for designing, sponsoring, and implementing biomedical studies involving human beings should always report what proportion of the patients included in studies were enrolled in the United States and what proportion were enrolled abroad.
- Similarly, all clinical biomedical study reports should consistently present demographic data on the number of patients invited to participate, the number of screen failures, and the number of people who consented and were enrolled. These demographic data should include an analysis of the total number of patients participating, and a breakdown of participants by race/ethnic group.
- All biomedical studies conducted among humans in the United States should provide a detailed report of the enrolled patients, including an analysis of the patient population by ethnicity, including the five major ethnic groups in the United States (non-Hispanic white, African American, Hispanic, Asian, and Native American).
- As an adjunct to Good Clinical Practice, the design and implementation of biomedical studies in humans should endeavor to match the ethnicity and race of the populations targeted for treatment, based upon the demographics of the disease under study.
- Whenever possible, enrollment in biomedical studies should take into account the enrollment size of racial/ethnic subpopulations of patients so that powered conclusions can be obtained via subpopulation statistical analysis.
- Safety and efficacy analyses of any new medical treatment, medication, medical device, or medical or surgical intervention should always include subpopulation analyses by race and ethnicity.
- The FDA should enforce existing policies that make the reporting of ethnicity of patient populations in clinical trials mandatory in all clinical trials intended for registration of new treatments. In addition, the FDA should consider issuing additional regulations that make it mandatory for all sponsors of clinical

trials submitted for new registration approval or for safety and efficacy monitoring, to include in these trials members of ethnic minorities in a proportion that matches the epidemiology of the disease studied.

- Government incentives should be considered for industry to adopt the practice of including ethnic minority patients in clinical trials. Such incentives should be proportional to the additional effort and expenditure incurred by industry and could be given in the form of patent extensions.
- Medical colleges in the United States should redouble efforts to increase the enrollment of all under-represented ethnic minorities. In addition, medical schools should continue to improve on the teaching of Good Clinical Practice[c] as part of their curricula. The only long-term solution to the under-representation of ethnic minority patients in clinical research and the paucity of minority physicians in biomedical research is to properly attract and educate more minority investigators.
- Government and industry sponsors of clinical trials should increase their efforts to effectively train, recruit, and retain community-based minority investigators. Access to clinical trials can best be offered to minority patients through practicing minority physicians in community-based settings. It is essential that this group of physicians have the necessary support to engage in conducting clinical research studies.
- All those involved with the solicitation, the review, and the acceptance of any manuscript reporting the results of such biomedical studies that involve human beings, including publishers, editorial boards, journal reviewers, government and regulatory agencies, reimbursement bodies, grant approval and renewal bodies, academic institutions, insurance agencies, and the like should reject any study data that do not include a concise and transparent report and analysis of ethnic subpopulations.

Notes

[a] Cardiovascular diseases that disproportionately afflict minorities are hypertension, stroke, congestive heart failure, and acute coronary disease; metabolic and endocrinology diseases are type II diabetes and respiratory diseases such as asthma; cancers are colorectal, prostate, and cervical; neuropsychiatric disorders are Alzheimer's, depression, and acute psychosis; infectious diseases occurring at higher rates are AIDS and HPV.

[b] The Office of Management and Budget (OMB) adopted a set of standards in 1977, titled "Directive No. 15, Race and Ethnic Standards for Federal Statistics and Administrative Reporting," to standardize classifications for record keeping, collection, and presentation of data on race and ethnicity in federal program administrative reporting and statistical activities (http://wonder.cdc.gov/wonder/help/populations/bridged-race/Directive15.html). The standards were revised in 1997, defining five minimum data categories for race: American Indian or Alaska Native, Asian, black or African American, Native Hawaiian or Other Pacific Islander, and white. Two data categories were defined for ethnicity: "Hispanic or Latino" and "Not Hispanic or Latino." The directive notes that "the racial and ethnic categories set forth in the standards should not be interpreted as being primarily biological or genetic in reference. Race and ethnicity may be thought of in terms of social and cultural characteristics as well as ancestry." (http://www.whitehouse.gov/omb/fedreg/1997standards.html). The Directive does not define how race or ethnicity is determined. Categorization most likely falls to self-description by subjects. Other shortfalls in the use of the terms for race and ethnicity are described by the American Anthropological Association (http://www.aaanet.org/gvt/ombdraft.htm). Nevertheless, these categories have been used in government-sponsored research and reporting, as well as in other independent research, to attempt understanding of the very real medical consequences of genetic variations in populations and, most important, these categories are the basis for describing the American population in census data that serve as an over-arching reference on the adequacy of clinical research vis-à-vis the majority population. Variations in ethnic and racial categories among different studies are not necessarily congruent, and individual studies need to be examined for how such categories are defined, even if the seem to be generally understood.

[c] The FDA specifically regulates clinical practice and clinical research conducted by biomedical entities including universities, corporations, government institutions, etc. See FDA Regulations Relating to Good Clinical Practice and Clinical Trials (http://www.fda.gov/oc/gcp/regulations.html).

Reference Cited in Text

1. Wendler D, Kington R, Madans J, Van Wye G, Christ-Schmidt H, et al. (2006) Are racial and ethnic minorities less willing to participate in health research? PLoS Med 3(2): e19: 201-10.

Additional References

Agency-wide Race and Ethnicity Working Group from the Office of the Commissioner (OC), the Center for Biologics Evaluation and Research (CBER), the Center for Drug Evaluation and Research (CDER) and the Center for devices and Radiological Health (CDRH) of the Food and Drug Administration: Guideline for Industry: Collection of Race and Ethnicity Data in Clinical Trials. U.S. Department of Health and Human Services, Food and Drug Administration, Clinical Medical; September 2005.

AHRQ. Addressing Racial and Ethnic Disparities in Health Care. Fact Sheet, February 2000. AHRQ Publication No. 00-PO41. Agency for Healthcare Research and Quality, Rockville, MD. http://www.ahrq.gov/research/disparit.htm.

American Cancer Society. Cancer Facts & Figures for African Americans 2005-2006. Atlanta: American Cancer Society, 2005.

Association of American Medical Colleges (AAMC) Report: Diversity in the Physician Workforce: Facts and Figures 2006. Published by the AAMC Division of Diversity Policy and Programs, Summer 2006; 2450 North St NW, Washington D.C. 20037-1127; Laura Castillo-Page, Editor.

Association of American Medical Colleges (AAMC) Report: Minorities in Medical Education: Facts and Figures 2005. Published by the AAMC Division of Diversity Policy and Programs, Summer 2005; 2450 North St NW, Washington D.C. 20037-1127; Laura Castillo-Page, Editor.

Branson RD, Davis K Jr, Butler KL. African Americans' participation in clinical research: importance, barriers, and solutions. Am J Surg. 2007 Jan;193(1):32-9; discussion 40.

Burchard EG, Ziv E, Coyle N, Gomez SL, Tang H, Karter AJ, Mountain JL, Perez-Stable EJ, Sheppard D, Risch N. The importance of race and ethnic background in biomedical research and clinical practice. N Engl J Med. 2003 Mar 20;348(12):1170-5.

Carolina Reyes, MD, Leticia Van de Putte, RPh, Adolph P. Falcón, MPP, Richard A. Levy, PhDGenes, Culture, and Medicines: Bridging Gaps in Treatment for Hispanic Americans. February 2004 by the National Alliance for Hispanic Health and the National Pharmaceutical Council.

Corbie-Smith G, Miller WC, Ransohoff DF. Interpretations of 'appropriate' minority inclusion in clinical research. Am J Med. 2004 Feb 15;116(4):249-52.

Corbie-Smith G, Moody-Ayers S, Thrasher AD. Closing the circle between minority inclusion in research and health disparities. Arch Intern Med. 2004 Jul 12;164(13):1362-4.

Corbie-Smith G, Thomas SB, St George DM. Distrust, race, and research. Arch Intern Med. 2002 Nov 25;162(21):2458-63.

Corbie-Smith G, Thomas SB, Williams MV, Moody-Ayers S. Attitudes and beliefs of African Americans toward participation in medical research. J Gen Intern Med. 1999 Sep;14(9):537-46.

Epstein AM. Health care in America--still too separate, not yet equal. N Engl J Med. 2004 Aug 5;351(6):603-5.

Evelyn B, Toigo T, Banks D, et al: Participation of racial/ethnic groups in clinical trials and race-related labeling: a review of new molecular entities approved 1995-1999. J Natl Med Assoc. 2001 Dec; 93(12 Suppl):18S-24S.

Ford JG, Howerton MW, Bolen S, Gary TL, Lai GY, Tilburt J, Gibbons MC, Baffi C, Wilson RF, Feuerstein CJ, Tanpitukpongse P, Powe NR, Bass EB. Knowledge and Access to Information on Recruitment of Underrepresented Populations to Cancer Clinical Trials. Evidence Report/Technology Assessment No. 122 (Prepared by the Johns Hopkins University Evidence based Practice Center under Contract No. 290-02-0018.) AHRQ Publication No. 05-E019-2. Rockville, MD. Agency for Healthcare Research and Quality. June 2005. Accessed 24 February 2007 at http://www.ahrq.gov/downloads/pub/evidence/pdf/recruitcantrials/recruit.pdf.

Ghafoor A, Jemal A, Cokkinides V, Cardinez C, Murray T, Samuels A, Thun MJ. Cancer statistics for African Americans. CA Cancer J Clin. 2002 Nov-Dec;52(6):326-41.

Gross CP, Filardo G, Mayne ST, Krumholz HM. The impact of socioeconomic status and race on trial participation for older women with breast cancer. Cancer. 2005 Feb 1;103(3):483-91.

Harrison RW 3rd. Impact of biomedical research on African Americans. J Natl Med Assoc. 2001 Mar;93(3 Suppl):6S-7S.

Katz RV, Russell SL, Kressin NR, Green BL, Wang MQ, James SA and Claudio C: The Tuskegee Legacy project: Willingness of minorities to participate in Biomedical research. J Health Care Poor Underserved. 2006 November;17(4):698-715.

Komaromy M, Grumbach K, Drake M, Vranizan K, Lurie N, Keane D and Bindman AB: The role of black and Hispanic physicians in providing health care for underserved populations. N Eng J Med. 1996;334:1305-10.

Lurie N. Health disparities—less, more action. N Engl J Med. 2005 Aug 18;353(7):727-9.

McDonald M. Medical research and ethnic minorities. Postgrad Med J. 2003 Mar;79(929):125-6.

Moy E, Bartman BA. Physician race and care of minority and medically indigent patients. JAMA. 1995;273:1515-20.

NIH. HIV Infection in Minority Populations. April 2005. Accessed 26 February 2007 at http://www.niaid.nih.gov/factsheets/Minor.htm.

NIH. NIH Policy on reporting race and ethnicity data: Subjects in clinical research. release date: August 8, 2001. Accessed 26 February 2007 at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-053.html.

Office of Special Populations and Research Training National Institute of Allergy and Infectious Diseases National Institutes of Health Department of Health and Human Services. Increasing Diversity in Clinical Trials: Best Practices. Health Disparities Symposium, October 2, 2003.

Owen, Diana. American Identity, Citizenship, and Multiculturalism. Presented at the German-American Conference cosponsored by the Bundeszenrale fur politische Bildung and the Center for Civic Education, September 11-16, 2005, Freiburg, Germany.

Risch N. Dissecting racial and ethnic differences. N Engl J Med. 2006 Jan 26;354(4):408-11.

Roberts M. Racial and ethnic differences in health insurance coverage and usual source of health care, 2002. Rockville, (MD): Agency for Healthcare Research and Quality; 2006. MEPS Chartbook No. 14. AHRQ Pub. No. 06-0004. Accessed online 24 February 2007 at http://www.meps.ahrq.gov/mepsweb/data_files/publications/cb14/cb14.pdf.

Shavers-Hornaday VL, Lynch CF, Burmeister LF, Torner JC. Why are African Americans under-represented in medical research studies? Impediments to participation. Ethn Health. 1997 Mar-Jun;2(1-2):31-45.

Suddendorf, RF Research on alcohol metabolism among Asians and its implications for understanding causes of alcoholism. Public Health Reports. 1989 Nov-Dec;104(6):615-20.

U.S. Census Bureau. Race and Hispanic or Latino Summary File. 2001. Reyes C, Van de Putte L, Falcón AP, Levy RA. Genes, culture and medicines: bridging gaps in treatment for Hispanic Americans. National Alliance for Hispanic Health. Washington DC; February 2004. United States Department of Health & Human Services; Agency for Healthcare Research and Quality (AHRQ); Access to Health Care. Table 2.1: People who have a usual primary care provider, by race/ethnicity, United States, 2004. Accessed 24 February 2007 at http://www.meps.ahrq.gov/mepsweb/data_stats/summ_tables/hc/acc/2004/acctocare_2_1_2004.htm.

United States Department of Health & Human Services; Agency for Healthcare Research and Quality (AHRQ); Racial and Ethnic Differences in Health Insurance Coverage and Usual Source of Health Care, 2002. Accessed 24 February 2007 at http://www.meps.ahrq.gov/mepsweb/data_files/publications/cb14/cb14.pdf.

NIH Policy for Inclusion of Minorities in Biomedical Research

Lawrence Agodoa, M.D.

Introduction

Overcoming persistent health disparities and promoting health for all Americans rank as our Nation's foremost health challenges. To overcome them, the National Institutes of Health (NIH) is supporting and conducting a wide range of research and seeking new knowledge, strategies, and methodologies about disease and disabilities. This new knowledge will continue to lead to innovative diagnostics, treatments, and preventive strategies to reduce, and eventually eliminate, health disparities.

NIH Strategic Plan to Eliminate Health Disparities

To meet this challenge, the Department of Health and Human Services instructed all of its agencies in 1999 to develop initiatives aimed at reducing and eventually eliminating health disparities. In addition, each of the Institutes and Centers (ICs) at the National Institutes of Health was mandated to develop minority health disparities strategic plans.

The initiatives described in each IC plan were to represent the major priorities and broad range of activities that the NIH collectively would undertake to reduce and ultimately eliminate health disparities. Each IC met the challenge and came up with a minority health disparities strategic plan. All of the plans across the NIH were coordinated by the National Center on Minority Health and Health Disparities (NCMHD), and formed the basis for a combined comprehensive NIH Health Disparities Strategic Plan. The plan is not merely a compilation of all the activities of the NIH entities, but an aggregation of primary areas of emphasis and activities conducted across the NIH. An evolving process, the strategic plan has been and will continue to be revised based on public comments received, public health need, scientific opportunity, changes in available funds, and other factors. The plan follows a methodological model, which presents mission, vision, goals, objectives, and programs for reducing and eventually eliminating health disparities.

The Strategic Plan is focused on three major goals:

Research—to advance the understanding of the development and progression of diseases and disabilities that contribute to health disparities in racial and ethnic minority populations and in other populations with health disparities, including the medically underserved, by increasing and diversifying biomedical, behavioral, social science, and health services research, as well as cultural, linguistic, and social epidemiology research conducted and supported by the NIH.

Research Capacity—to increase minority health and health disparity research training, career development, and institutional research capacity and infrastructure.

Community Outreach, Information Dissemination, and Public Health Education—to ensure the public, health-care professionals, and research communities are informed and educated concerning the latest advances in minority health and health disparities research.

Objectives—The table on page 13 summarizes the specific objectives of each of the major goals.

Initiatives have been developed to support these objectives. All of these many initiatives cut across a variety of areas representing a myriad of diseases, disabilities, and organizational boundaries. The initiatives represent a trans-agency commitment to exploring and solving many of the health disparities problems faced by disadvantaged communities.

Ensuing reaction and comments from the public in response to the goals and objectives of the NIH strategic plan resulted in the following major themes:

- Increase the number of health disparities populations studied by the NIH.
- Use racially and culturally sensitive and appropriate communication and ensure that all communications with populations and their sub-groups that have health disparities are sensitive to their needs and perspectives.
- Expand the scope of scientific inquiry to include cultural, psychological, behavioral, social, racial, and gender-based influences on health and study access to health care. Produce accurate "health disparities" definitions and data.
- Improve research infrastructure at minority academic institutions.
- Strengthen the capacity of minority communities by

Objectives of NIH Strategic Plan to Eliminate Health Disparities

RESEARCH OBJECTIVES	RESEARCH CAPACITY OBJECTIVES	OUTREACH OBJECTIVES
• Advance understanding of the development and progression of diseases and disabilities that contribute to health disparities • Develop new or improved approaches for detecting or diagnosing the onset or progression of diseases and disabilities that contribute to health disparities • Develop new or improved approaches for preventing or delaying the onset or progression of diseases and disabilities that contribute to health disparities • Develop new or improved approaches for treating diseases and disabilities that contribute to health disparities • In partnership with other agencies of DHHS, advance understanding of the multifactorial causes of health disparities, including non-biological bases of disease incidence and progression	• Increase the number of participants in clinical trials from racial and ethnic minority populations and other health disparity populations • Expand opportunities in research training and career development for, and provide research supplements to, research investigators from racial and ethnic minority populations and other health disparity populations • Increase the number of researchers conducting health disparities research • Increase funding support for construction and renovation of research facilities across the Nation aimed at enhancing the ability of these institutions to conduct health disparities research • Provide increased funding at institutions across the country for resources, new equipment, and shared equipment programs for use in health disparities research • Increase representation in peer review from racial and ethnic minority populations and other health disparity populations • Promote the development of inter-institutional partnerships between historically research intensive and historically minority serving institutions that seek to build research infrastructure • Improve research data collection systems, and enhance data quality regarding health disparities, and develop uniform data systems that facilitate strategies for the elimination of health disparities • In collaboration with schools and programs of public health, state and local health departments, and academic health departments, support and promote community-based participatory research	• Provide the latest research-based information to healthcare providers to enhance the care provided to individuals within racial and ethnic minority populations and other health disparity populations • Facilitate the incorporation of science-based information into the curricula of medical and allied health professions schools, theological education institutions, public health schools, and into continuing education activities of health professionals • Maintain ongoing communication linkages and partnerships with community-based and faith-based organizations, health care associations, foundations and academic institutions, and foster dialogue with racial and ethnic minority populations and other health disparity populations, including the underserved • Develop computer databases and internet resources to disseminate current information about scientific research and discoveries and other activities regarding health disparities • Develop targeted public health education programs focused on particular disease areas in order to reach those individuals within racial and ethnic minority populations and other health disparity populations who experience health disparities within these disease areas • Facilitate, document and disseminate practical strategies responsive to the health care needs, and appropriate to the cultural and linguistic needs, of communities throughout the United States • Collaborate with public health and other health oriented policy centers to translate research findings into policy documents that can be used by policy groups and other stakeholders to explain new discoveries from a policy perspective to decision makers

broadening partnerships and leveraging resources available from professional associations, health care organizations, academic institutions, and other community members that serve minority communities.

- Distribute NIH resources equitably across all population groups by increasing research regarding men, American Indians and Alaska Natives, Hispanics, and groups from Southeast Asia.

Multifactorial Basis of Health Disparities

The causes of health disparities are posited to be multifactorial and hence require a coordinated and interdisciplinary approach to eliminate them. With the exception of race, many of these factors apply to non-ethnic underserved populations as well. The common denominator in the latter case is related to low socioeconomic status and the protean effects of poverty on health.

Although many factors contribute to overall health disparities, and NIH is addressing several of these factors, the following are more detailed descriptions of those that could be dealt with by increasing minority participation in clinical research:

Biology—Even after controlling for socioeconomic status there seem to be factors that further influence disease states in racial and ethnic populations. Some of this residual effect may be biological in nature. For instance, differences in socioeconomic status do not completely explain the higher rates of hypertension, glaucoma, and lupus in African Americans. "Thrifty genes" and other predisposing genetic factors have been proposed to explain the epidemic of obesity and diabetes in Pima Indians. Biological differences seem responsible for different rates of drug metabolism in various populations and may also explain why immunosuppressive agents appear to be less effective in African Americans.

Access and Quality of Health Care—Health care access and quality—and information about and access to clinical trials—are often substandard in the same populations that suffer from health disparities. Lack of access may lead to failure in disease prevention, delayed detection, and inadequate treatment. Lack of access to clinical trials contributes to an under-representation of ethnic and racial minorities in those trials and to a lack of information on the effects of treatments in those populations. In the United States, racial minorities and other groups with health disparities suffer from barriers to medical care for multiple reasons, i.e., lack of insurance, unemployment, language barriers, travel barriers, immigration status, and issues related to culture, trust, and discrimination. The same barriers apply in the arena of clinical trial participation. Though it is necessary to eliminate these barriers, equalizing access will not be sufficient to eliminate health disparities. Even in countries that have optimized and equalized access, Britain and Finland for example, health disparities persist and closely track socioeconomic status.

Socioeconomic Status/Education Level—There is a large body of literature documenting the inverse association between low socioeconomic status and good health. Evans and Kim[1] examined the longitudinal relations between duration of poverty since birth, cumulative risk exposure, and physiological stress in 200 13-year olds and showed that the greater the number of years in poverty, the more elevated was overnight cortisol and the more dysregulated was the cardiovascular response. Similarly, Delva et. al.[2] using cross-sectional survey data from nationally representative samples from 1998 to 2003 showed over-representation of youth at risk of overweight or overweight among racial and ethnic minority youth, similar to the morbidity of overweight and obesity-related health problems in these populations. The negative health effects of depressed socioeconomic status are relevant to many racial and ethnic minorities, as well as to underserved white populations.

Cultural Considerations—Cultural practices often involve diet and other behaviors that influence health status. In addition, cultural factors may include alternative methods of healing that may conflict with mainstream medicine. Many racial and ethnic minority patients who employ traditional methods of healing feel uncomfortable informing non-ethnic caregivers of these modalities, which may include pharmacologically active herbs. Increasing the number of minority researchers and practitioners who take part in clinical trials is one approach to increasing the ease and comfort level of minority trial volunteers.

Policy for Inclusion of Minorities in Biomedical Research

Within the context of health disparities, NIH and the research communities it serves have long realized that racial and ethnic minorities in the United States are significantly disadvantaged in health and disease. However, the com-

petitive nature of obtaining support for clinical studies, especially clinical trials, may have been a disincentive for investigators to make special efforts to include hard-to-reach populations and communities, especially minorities and women, for inclusion in the study population. Realizing this negative practice, the NIH has established a policy that would deny funding to any proposed study that does not have an adequate inclusion plan. Some of the specifics of the guidelines follow.

NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research

In March of 1994, the NIH, in response to the NIH Revitalization Act of 1993, revised its policy on the inclusion of women and minorities as clinical research subjects. Since then, the NIH policy has been revised twice as necessary for clarification. This summary is of the current NIH policy and guidelines on the inclusion of women and minorities in clinical research. In June 2001, NIH adopted the definition of clinical research as:

- Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are *in vitro* studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes:
    - o Mechanisms of human disease.
    - o Therapeutic interventions.
    - o Clinical trials.
    - o Development of new technologies.
- Epidemiologic and behavioral studies.
- Outcomes research and health services research.

A primary aim of research is to provide scientific evidence leading to a change in health policy or standard of care. Decisions regarding such changes are often made at the phase III clinical trial stage, which typically follows several prior stages of clinical research studies. It is imperative to determine whether the intervention or therapy being studied affects women, men, or members of minority groups and their subpopulations differently so that appropriate policies may be implemented.

The NIH Revitalization Act of 1993 mandated that NIH-supported clinical research include adequate numbers of women and minorities to allow valid analysis of the data for differences of effect due to sex and/or race. Under the legislation, NIH bears responsibility for ensuring adequate diversity in clinical research, including the following:

- Ensure that women and members of minorities and their subpopulations are included in all human subject research.
- In phase III clinical trials, ensure that sufficient women and minorities and their subpopulations are included such that valid analyses of differences in intervention effect can be accomplished.
- Disallow cost as an acceptable reason for excluding these groups.
- Initiate programs and support for outreach efforts to recruit these groups into clinical studies.

Along with its policy, the NIH established guidelines for clinical investigators and review panels to ensure compliance with the new regulations. The policy requires that sex and race be given consideration at every stage of clinical research, and the guidelines are designed to help those responsible for providing this consideration determine the best mechanisms to accomplish it.

The Policy

The inclusion of women and members of minority groups and their subpopulations must be addressed in developing a research design appropriate to the scientific objectives of the study. At stages prior to phase III clinical trials, NIH guidelines state that:

- The research plan should describe the composition of the proposed study population in terms of gender and racial/ethnic group, and provide a rationale for selection of such subjects. Such a plan should contain a description of the proposed outreach programs for recruiting women and minorities as participants.

Once the phase III clinical trial stage has been reached, NIH guidelines are more specific, to comply with the regulations set forth in the 1993 law. At this stage, evidence must be reviewed to show whether clinically important sex or race/ethnicity differences in the intervention effect are to be expected. This evidence may include, but is not limited to, data derived from prior animal studies, clinical observations, metabolic studies, genetic studies,

pharmacology studies, and observational, natural history, epidemiology, and other relevant studies.

If the data from prior studies strongly support no significant differences[1] of clinical or public health importance in intervention effect between subgroups, then sex or race/ethnicity is not required as subject selection criteria. However, the inclusion of sex or racial/ethnic subgroups is still strongly encouraged.

There are two instances in which phase III clinical trials are required to be designed to study sex or race/ethnicity differences:

- If the data from prior studies strongly indicate the existence of significant differences of clinical or public health importance in intervention effect among subgroups (gender and/or racial/ethnic subgroups), the primary question(s) to be addressed by the proposed phase III trial, and the design of that trial, must specifically accommodate this. For example, if men and women are thought to respond differently to an intervention, then the phase III trial must be designed to answer two separate primary questions, one for men and the other for women, with adequate sample size for each.
- If the data from prior studies neither strongly support nor strongly negate the existence of significant differences of clinical or public health importance in intervention effect between subgroups, then the phase III trial will be required to include sufficient and appropriate entry of gender and racial/ethnic subgroups, so that valid analysis[2] of the intervention effect in subgroups can be performed. However, the trial will not be required to provide high statistical power for each subgroup.

[1] For purposes of this policy, a "significant difference" is a difference that is of clinical or public health importance, based on substantial scientific data.

[2] The term "valid analysis" means an unbiased assessment. Such an assessment will, on average, yield the correct estimate of the difference in outcomes between two groups of subjects. Valid analysis can and should be conducted for both small and large studies. A valid analysis does not need to have a high statistical power for detecting a stated effect.

Cost is not an acceptable reason to exclude women and minorities from clinical trials. NIH funding components do not award any grant, cooperative agreement or contract, or support any intramural project, which does not comply with this policy. Investigators are required to report annually on enrollment of women and men, and on the race and ethnicity of research participants.

The Guidelines

Guidelines were established for all participants, including NIH staff, principal investigators, peer review groups, and institutional review boards (IRBs).

Guidelines for Regulators

NIH staff is required to provide educational opportunities for investigators concerning the policy; to monitor its implementation during the development, review, award, and conduct of research; and to manage the NIH research portfolio to comply with the policy. Institute/Center directors and the director of the NIH are required to approve any exceptions to the policy.

Initial peer review groups are required to incorporate all of the following into their final evaluations of proposals:

- Evaluation of the proposed research plan for the inclusion of minorities and both genders for appropriate representation.
- Justification for limited representation or exclusion.
- Adequacy of clinical trial design to measure differences when warranted.
- Plans for outreach/recruitment of trial participants.

IRBs are required to consider and evaluate the implementation of the policy and guidelines in the context of human subjects protection and FDA regulations.

Guidelines for Researchers

The guidelines for investigators emphasize not only a rigorous analysis of any correlation between sex or race/ethnicity and their area of research, but also the need to establish strong relationships with the community in order to maintain a diverse volunteer population. The following is taken directly from the NIH guidelines:

> Principal investigators should assess the theoretical and/or scientific linkages between gender, race/ethnicity, and their topic of study. Following this assessment, the principal investigator and the applicant institution will address the policy in each application and proposal, providing the required information on inclusion of women and minorities and their subpopulations in

research projects, and any required justifications for exceptions to the policy. Depending on the purpose of the study, NIH recognizes that a single study may not include all minority groups.

Investigators and their staff(s) are urged to develop appropriate and culturally sensitive outreach programs and activities commensurate with the goals of the study. The objective should be to actively recruit the most diverse study population consistent with the purposes of the research project. Indeed, the

purpose should be to establish a relationship between the investigator(s) and staff(s) and populations and community(ies) of interest such that mutual benefit is derived for participants in the study. Investigator(s) and staff(s) should take precautionary measures to ensure that ethical concerns are clearly noted, such that there is minimal possibility of coercion or undue influence in the incentives or rewards offered in recruiting into or retaining participants in studies. It is also the responsibility of the IRBs to address these ethical concerns. Furthermore, while the statute focuses on recruitment outreach, NIH staff underscore the need to appropriately retain participants in clinical studies, and thus, the outreach programs and activities should address both recruitment and retention.

To assist investigators and potential study participants, NIH staff have prepared a notebook, **"NIH Outreach Notebook on the Inclusion of Women and Minorities in Biomedical and Behavioral Research."** The notebook addresses both recruitment and retention of women and minorities in clinical studies, provides relevant references and case studies, and discusses ethical issues. It is not intended as a definitive text on this subject, but should assist investigators in their consideration of an appropriate plan for recruiting and retaining participants in clinical studies.

Determining Race and Ethnicity

In 2001, NIH updated its categories defining race and ethnicity to follow those outlined in the Office of Management and Budget (OMB) Directive No. 15. NIH makes clear that these categories are not ideal in the gathering and interpreting of scientific data with the following statement: **The categories in this classification are social-political constructs and should not be interpreted as anthropological in nature.** Nonetheless, NIH uses these categories because they were standardized in this directive to allow easy comparison of data collected across federal agencies and in national health databases. NIH intends that investigators use the racial and ethnic categories in OMB Directive No. 15 as basic guidance, while remaining cognizant of the distinction based on cultural heritage.

A minority group is a readily identifiable subset of the U.S. population that is distinguished by racial, ethnic, and/or cultural heritage. Minority groups include:

- American Indian or Alaskan Native: A person having origins in any of the original peoples of North America, and who maintains cultural identification through tribal affiliation or community recognition.
- Asian or Pacific Islander: A person having origins in any of the original peoples of the Far East, Southeast Asia, the Indian subcontinent, or the Pacific Islands. This area includes, for example, China, India, Japan, Korea, the Philippine Islands and Samoa.
- Black, not of Hispanic Origin: A person having origins in any of the black racial groups of Africa.
- Hispanic: A person of Mexican, Puerto Rican, Cuban, Central or South American or other Spanish culture or origin, regardless of race.

Each minority group contains subpopulations that are delimited by geographic origins, national origins, and/or cultural differences. It is recognized that there are different ways of defining and reporting racial and ethnic population and subpopulation data. The assignation of an individual to a population group depends upon self-reporting of specific racial and ethnic origin. Attention to subpopulations also applies to individuals of mixed racial and/or ethnic parentage. Researchers should be cognizant of the possibility that these racial/ethnic combinations may have biomedical and/or cultural implications related to the scientific question under study.

NIH recognizes both the diversity of the U.S. population and that changing demographics are reflected in the changing racial and ethnic composition of the population. The terms "minority groups" and "minority subpopulations" are meant to be inclusive, rather than exclusive, of differing racial and ethnic categories. The majority group is defined as white, not of Hispanic Origin: A person having origins in any of the original peoples of Europe, North Africa, or the Middle East.

Discussion

The issues of designing significantly diverse clinical research studies are vast and varied and are often specific to the stage of research. Those considerations are also outside the scope of this document, which is focused on outlining recommendations for improving the recruitment and retention of minorities in clinical trials in order to support the goal of adequate data collection to determine effectiveness of treatments, interventions, and diagnoses in minority populations. As a result, this discussion will center on this specific concern to the exclusion of other considerations in the design and review of clinical research proposals.

The NIH's definition of clinical research was broadened to include all biomedical and behavioral research involving human subjects. This broad definition addresses the need to obtain data about minorities and both sexes early in the research process, providing valuable information for designing clinical trials to include adequate representation of population subsets when warranted. Investigators in early stages of clinical research are requested to consider the types of information concerning sex and minority groups that will be required when designing future phase III clinical trials, and to try to obtain it in their earlier stages of research involving human subjects.

Although the inclusion of minority subpopulations in research is a complex and challenging issue, it is nonetheless necessary in order to collect data on subpopulations where knowledge gaps exist. Researchers must consider the inclusion of subpopulations in all stages of research design. In meeting this objective, they should be aware of concurrent research that includes specific subpopulations and consider potential collaborations that may result in complementary subpopulation data. A complex issue arises over how broad or narrow the division into different subgroups should be, given the purpose of the research. Emphasis should be placed on including subpopulations in which the disease manifests itself or the intervention operates in an appreciably different way.

An important concern is the appropriate representation of minority groups in research, especially in geographical locations that may have limited numbers of racial/ethnic population groups available for study. The investigator must consider this in terms of the purpose of the research and other factors, such as the size of the study, relevant characteristics of the disease, disorder or condition, and the feasibility of establishing a collaboration, consortium, or some other arrangement to include minority groups. A justification is required if representation is limited.

NIH interprets the statute in a manner that leads to feasible and real improvements in the representation of different racial/ethnic groups in research and places emphasis on research in those subpopulations disproportionately affected by certain diseases or disorders.

References Cited in Text

1. Evans GW, Kim P: Childhood poverty and health: cumulative risk exposure and stress dysregulation. Psychol Sci. 18 (11):953-7, 2007.

2. Delva J, Johnston LD, and O'Malley PM: The epidemiology of overweight and related lifestyle behaviors: racial/ethnic and socioeconomic status differences among American youth. Am J Prev Med. 33:S178-86, 2007.

Additional References

Strategic Research Plan and Budget to Reduce and Ultimately Eliminate Health Disparities, Fiscal Years 2002-2006 at http://ncmhd.nih.gov/our_programs/strategic/volumes.asp.

NIH GUIDELINES ON THE INCLUSION OF WOMEN AND MINORITIES AS SUBJECTS IN CLINICAL RESEARCH—Amended Guidelines at http://grants.nih.gov/grants/funding/women_min/guidelines_update.htm.

United States Food and Drug Administration: Current and Proposed Roles

G. Alexander Fleming, M.D.

As the federal agency responsible for regulating therapeutic research and marketed health products, the U.S. Food and Drug Administration (FDA) has the lead role in encouraging and verifying the collection of ethnic data from clinical trials and other investigations. One of FDA's core missions is to ensure that drugs and other health products are used appropriately in all people for whom the products are indicated. Translating demographic data from therapeutic trials into product labeling and other resources that improve the safety and efficacy of drugs in any relevant population subgroup is part of that mission.

The influence of gender on drug responses has received considerable FDA attention as an important demographic factor and has prompted multiple actions by the Agency. FDA has recognized the importance of ethnic subgroups for clinical therapeutics in its 2005 guidance on the collection of race and ethnicity data, but has not taken any further steps to encourage the collection and use of these data. The existence of this document may give the impression that FDA has dealt comprehensively with the role of ethnic and racial data in therapeutic development and clinical therapeutics. However, this guidance is little more than a suggestion for how racial and ethnic data should be categorized. It does not attempt to set out any definition or principles for establishing the composition of an adequately diverse clinical trial. The following wording is taken directly from the published document:

> This guidance does not address the level of participation of racial and ethnic groups in clinical trials. For questions related to the level of participation or the size of a study sponsors should consult with the review division prior to the start of a study.

As in any FDA guidance, the racial and ethnic guidance stresses that it "represents FDA's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations." It is further stated that:

> FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Although pharmaceutical companies and contract research organizations (CROs) take FDA guidances seriously, these documents have limited impact compared to regulations. Guidances are important tools for advancing the practice of therapeutic development because they can be put in place much quicker than can regulations or laws. A guidance is often an intermediate step in developing a regulation. FDA has been able to effect substantial changes with the guidance mechanism. The benefits of using racial and ethnic data in the development and clinical use of therapies can be realized by a more specific update of or successor to the current guidance. A longer-term goal would be to develop a comprehensive regulation that replaces the first regulation to specify the analysis of population subsets, which became effective in 1985. This regulation, now found under 21 CFR 314.50, calls for evidence to support the dosage and administration section of the drug product labeling, including support for the dosage and dose interval recommended and modifications for specific subgroups (e.g., pediatrics, geriatrics, patients with renal failure). This regulation could be updated to integrate appropriate standards for other subgroups including gender, racial and ethnic, and others based on easily identifiable phenotypes.

The ultimate aim of therapeutic evaluation and clinical practice is to apply the most appropriate means available for optimizing the selection of a treatment and its dosing for the individual. This will be a rapidly evolving proposition as technologies improve for relating pharmacologic responses to increasingly smaller segments of genomic DNA. However, for the foreseeable future, the field of pharmacogenomics will not supplant the value of data from racial, ethnic, and other easily identified phenotypes for individualizing the selection and dosing of medications. The appropriate legislation, in order to be durable, should mandate the general requirements and make room for the details to be based on the evolving science.

FDA has a leading responsibility in the following areas as part of the effort to maximize the health and economic values of determining differences in response to treatment across racial and ethnic groups.

Improving Guidance to Industry and Investigators

The current FDA guidance has two major deficiencies, which are in effect acknowledged in the document. First, the guidance does not provide any information that would help industry and investigators understand what representation of racial and ethnic subgroups within a development program would be adequate for analytical and regulatory purposes. Though the relevant clinical, biostatistical, and basic science considerations are complex, all stakeholders will benefit from understanding the general principles and expectations that are applied by FDA. The Agency will also benefit from reducing the inefficiency and inconsistency entailed in placing the burden on each of its 16 review divisions to customize a set of requirements for each sponsor, as is prescribed in the current guidance.

The current guidance recommends a racial and ethnic classification system that has no scientific or clinical basis. These groups are defined on the basis of sociologic and lingual attributes and therefore cannot be expected to be predictive of biologic response. With the help of experts, FDA should develop a practical means of identifying racial and ethnic identity based on an appropriate classification system. A decimal coding system analogous to the approach used to classify adverse events could be devised for use in both the clinical care and clinical trial settings. Such a system could encompass other important phenotypic attributes such as gender, age strata, or organ function impairment. Such a systematic and numerical approach would facilitate collection and meta-analyses of large amounts of data. Complex interactions among these different attributes could thereby be detected in correlating pharmacologic responses with genetic make up. This approach would provide correlative responses from a cohort that is most like a given individual. Because such a system would affect a large number of government agencies within and outside the Public Health Service and a number of other stakeholder organizations, this should be a broad-based effort.

Facilitating the Acquisition of Racial and Ethnic Data

Setting targets by FDA for racial and ethnic representation in clinical trials will not alone suffice to achieve these goals. The Agency can promote collection of these data by helping industry to develop standardized approaches to be used by all parties involved in the clinical trial process. It can encourage, and to some extent support, the training of minority investigators who are more likely to recruit members of racial and ethnic groups into their trials. FDA could also provide incentives for going beyond a minimal standard in collecting and utilizing such data. Existing legislation provides for additional market exclusivity for orphan drug indications and pediatric data. Congress could allow FDA to provide similar incentives to pharmaceutical companies for substantial improvement in the understanding of race or ethnicity as a determinant in the response to a given drug. The Agency could also award exclusivity for an indication confined to a specific racial or ethnic group. The isosorbide dinitrate-hydralazine combination drug product, BiDil® (NitroMed) was approved by the FDA in 2006 for self-described African Americans with heart failure. This was FDA's first racial-specific indication approval. Providing exclusivity on this basis will encourage other such indications to follow and thereby address unmet clinical need.

Advancing the Value of Racial and Ethnic Data

FDA can take the lead in developing standard data management and analytical approaches for use by all sponsors. Coupled with a standardized and robust classification system, these analytical approaches will enable sponsors to maximize the value of databoth within and across trials in a therapeutic development program. FDA is in a unique position to analyze racial and ethnic data from multiple drugs within and across related therapeutic classes, which could uncover predictors of response that would not otherwise be possible.

Education and Encouragement of Health Care Professionals and Consumers

Consistent with one of its core missions, the FDA can improve knowledge among prescribers and other health care professionals about how to use the results of racial and ethnic data from clinical trials to better individualize therapies for their patients. This educational effort should not occur in isolation, but should be part of an integrated approach to individualizing therapy to the full extent possible using all relevant subgroup data. FDA can, likewise, help to inform patients about the importance of understanding that constitutional makeup, including ethnic and racial background, can make a difference in their responses to medications.

The Community Perspective

Naomi Bitow, M.P.H., Deborah Prothrow-Stith, M.D., and Brian K. Gibbs, Ph.D., M.P.A., OTR/L

Introduction

The elimination of racial/ethnic disparities in health status and health care, major goals of *Healthy People 2010*, poses great challenges. Certain subsets of the population experience wide disparities in access to health services, outcomes of health care, and higher relative risk of poor health than the population as a whole. At the same time, demographic shifts are occurring in the United States that will result in these populations becoming the majority within the twenty-first century.[1]

Addressing factors that endanger the health of minority populations will demand broad strategic efforts directed at improving public and provider education, prevention of violence and common diseases, research on diseases that disproportionately affect minorities, and policy and environmental changes that facilitate healthy living for all our citizens. Progress in public health can arise only through mutually respectful, reciprocal relationships among researchers, community members, and policy makers.

Public health endeavors must be approached with the input and support of those who will be affected. In other words, "communities must be involved as partners in the design, implementation, and evaluation of interventions. The best intervention results have been achieved when people who benefit from interventions work closely with researchers and public health practitioners… A partnership between [researchers and communities] offers the best chance to bridge the divide."[2 (p. 668), 3 (pp. 5–6)]

There are many sources of disparities in health status between minorities and non-minorities, all of which contribute to the overall discrepancy in disease prevalence. Some commonly discussed reasons for disparities are a lack of access to health services and a difference in the quality of treatment within the health care system. However, another less well considered source of discrepancies in health status, specifically at the level of disease prevalence, is a difference in response to therapeutic interventions by different subpopulations. The concept of these differences is relatively new and is only well studied for certain treatments, the most widely publicized of which may be the response of African American patients to BiDil®. For the most part there is a dearth of race- and ethnicity-specific information from clinical trials examining the effects of drugs or interventions. In other words, minority populations have not been adequately studied to determine whether treatments and interventions are more or less effective for them than for Caucasian populations.

To accurately evaluate the response of minority populations to treatments under development, there must be adequate representation of these populations in clinical trials. This requires that minorities be informed of clinical trials available to them and invited to participate. It also requires that they be willing and able to participate. Although studies have shown that minorities are largely willing to participate in clinical trials—especially when invited by their own physicians—many barriers exist in both the communication of opportunities to minority communities and in the ability of minority individuals to participate. Tearing down both sets of barriers requires community outreach and cultural activism. (See Appendix I for the personal experience of an academic researcher and Appendix II for a description of common impediments and best practices for addressing them.)

The Importance of Outreach Programs and Activities in Reducing Health Disparities

Cultural activism is a form of political action practiced by many grassroots groups to transform communities around social issues. Cultural activism gives a voice to people. It is a strategy for social change and liberation, gaining political power, and building political unity. Cultural activism develops a community by connecting diverse people, and converts community members from spectators to activists. The civil rights movement, the struggles for women's rights, and the fight against AIDS are examples of organizing to facilitate social change and to reduce health disparities. Using a community's culture to promote healthy lifestyles and behaviors can be a powerful tool for building and empowering that community. The creation and reaffirmation of community culture can advance grassroots organizing for reducing health disparities. Identifying shared history is a way of building community solidarity. The crisis in health disparities is a potentially unifying phenomenon that can

link seemingly separate issues and peoples. How will people imagine a society that transcends racism, sexism, and class? Social transformation means rethinking these relations.[2]

A Community Model: Cherishing Our Hearts and Souls (Roxbury, Mass.)

Although much has been written about the existence and causes of health disparities, very little progress has been made in devising and implementing public health programs that are actually able to reduce those disparities. Cherishing Our Hearts and Souls Coalition (COHS) is a community-based initiative in Roxbury, Mass., a neighborhood representing 8% of Boston residents and with a large minority population. 2000 census data from Roxbury reflected 51.5% black (non-Hispanic), 25.5% Hispanic, 15% white, and 4.5% Asian. Roxbury's residents fare worse in many health issues than do Bostonians overall or even black Bostonians, who as a group fare worse than white Bostonians. That is to say, there is a high level of disparity in health and health care in Roxbury compared to that found in nearby neighborhoods. COHS is addressing these disparities in Roxbury.

COHS is an exciting partnership of academics, individual residents, and community organizations. It works on disparities in health and health care through social transformation[4] and building social capital within communities—Roxbury being one of them. The theoretical basis of COHS is the understanding and addressing of racism as a necessary strategy for reducing health disparities, and appreciating the lessons learned from successful contemporary social transformation models. COHS focuses on the African American population of Roxbury to identify specific explanations for disparities in their health status.

In collaboration with community-based organizations, health centers, activists, educators, schools, and youth service programs, COHS works with the Harvard School of Public Health's Program to Eliminate Health Disparities (HSPH/PEHD) to infuse public health practice and education with the knowledge, strategies, and energy found in historically successful social movements, including the civil rights movement, union organizing, the international women's movement, and environmental justice. Through the principles of community-based participatory research (CBPR), COHS is committed to transforming the health status of the residents of Roxbury and the nation.

COHS consists of four clusters:

1) Anti-Racism Cluster.
2) Clinical Care and Research Cluster.
3) Health Promotion Cluster.
4) Youth Cluster.

Coalition members view each of these as a significant area for improving the health and health care experiences of residents and the health care professionals who serve Roxbury. HSPH provides assistance to each cluster, ensures coordination and integration of overall COHS-related goals and activities, maintains the COHS database, sets bimonthly COHS coalition meetings, serves as the COHS point of contact, leverages coalition-building resources in the pursuit of private foundation or federal funding opportunities, and coordinates community trainings and information dissemination activities.

To translate public health research into practice, COHS relies on the Clinical Care and Research Cluster (CCRC) for direction. CCRC's mission is to improve Roxbury residents' access to community-based research opportunities and information about high-quality clinical care, to increase the number of people of color who participate in clinical trials and pursue careers in health care, and to ensure that community perspectives are represented in emerging health policy, health-disparities research, and training opportunities. This mission is based on a belief that the health care community must be responsive to system, institutional, interpersonal, and individual factors that contribute to health disparities. These include but are not limited to the lack of resources and funding for outreach, the inadequacy of hospital interpreter services, poorly addressed issues related to immigration, and differential treatment, racism, and feelings of mistrust in clinical settings, including in clinical research settings.

The CCRC has been instrumental in contributing to the establishment of the Roxbury Community Research Advisory Board (CRAB), which consists of community leaders and residents whose goal is to improve community understanding of, and responsiveness to, community-based and clinical research. The mission of the CRAB is to connect Roxbury residents to the Harvard School of Public Health in a mutually beneficial effort to increase knowledge and promote understanding about how community-based participatory research can help eliminate disparities in health and health care, thereby improving the health and well-being of people of color and the poor.

The CCRC has also contributed to several clinical-care, research, and training initiatives. In 2003, the Center for Healthy Options and Innovative Community Empowerment (CHOICE), an NIH-NCMHD EXPORT Center, was established, in part to create the foundation of an important prospective cohort study of hypertension in two predominantly African American populations, one rural and the other urban. CHOICE, a 4-year research, outreach, and training initiative, is a partnership of the Harvard School of Public Health, Florida A & M University, Gadsden County, Florida, and the Cherishing Our Hearts and Souls of Roxbury. In 2005, the W.K. Kellogg Foundation awarded funding to COHS to conduct training sessions for Roxbury residents and providers and patients of Roxbury neighborhood health centers. These sessions addressed the relationship between heart disease and racism with the goal of developing new strategies for prevention. In February 2006, COHS received a 3-year award from Education Network to Advance Clinical Trails (ENACCT) to establish *Breaking It Down*: *Our Health Our Way*. With this grant, COHS/Roxbury became one of three national pilot educational program sites selected to identify, implement, and validate innovative approaches to cancer clinical trials education, outreach, and recruitment to improve outcomes for all. Both the Roxbury CRAB and the *Breaking It Down: Our Health Our Way* initiatives include training on social justice, the ethics of research involving cancer, and attention to other health disparities.

Lessons Learned

1. Activism on the part of knowledgeable professionals can help to inspire and empower a community.
   - Don't shy away from your role as a partner—share, share, share, and keep coming back to the table—even when it's tough.

2. Longevity and accountability within professional community partnerships can restore faith and hope.
   - Professional leadership is not enough—community activism is essential to social transformation.
   - Stay involved or be clear about the limitations of your involvement.

3. Successful social transformation models provide evidence of the possibility for change and strategies to model.
   - Find your hope in a community's prior successes—listen, listen, listen.

4. An asset-based approach to partnership uses everyone's strengths.
   - Never stop looking for the resources others bring to the table.
   - Always seek a partner to help you analyze and act on your findings.

5. Strategies outside of public health are essential to success.
   - Learn the history (and the language if you can), read the newspapers and listen, listen, listen.

6. Building an infrastructure for community participation enhances sustainability.
   - Career development and training for partners should be part of your formal goals.

7. Creative out-of-the-box thinking is essential.
   - Accept that outsiders cannot fully understand community dynamics—though this is not an excuse for staying uninvolved.
   - Speak about white privilege and recognize that privilege is continually operating to some degree, creating power imbalance.

8. The research process can be used to mobilize and advocate for change.
   - Aim for accurate race/ethnicity data collection.
   - Acknowledge the diversity within racial and ethnic groups.
   - Examine the role of racism in diminishing the health of entire populations.

Recommendations from the Community Perspective

Recommendation 1—*Minority Health Care Professional Recruitment and Retention*. Assist in the racial and ethnic diversification of the health workforce pipeline for the local community by initiating new, and supplementing existing, after-school/weekend junior-high and high-school math and science programs that incorporate an understanding of nutrition and teach the principles of a "healthy lifestyle" important to disease prevention. Co-sponsor tutoring and mentoring programs between public school systems, undergraduate, graduate, and professional degree programs, health care, public health, and business communities. Sponsor health career fairs or institutes and identify new, or supplement existing, minority health or health disparities fellowship training programs. These programs will increase the likelihood of recruiting the diverse health care workforce so essential to the success of clinical research endeavors.

Recommendation 2—P*romote Responsive Data Collection and Reporting on Race and Ethnicity*. Establish and support a local area data-collection work group on race and ethnicity composed of data users, state and local health departments, and collectors of federal data (i.e., funeral directors, hospitals, nursing homes, and census bureaus), local practitioners, health-system administrators, academic training institutions, community leaders, and elected officials. More specifically, encourage and support the collection of race and ethnicity data among its funded programs, maintain annual profiles and reports on racial and ethnic disparities in health and health care at the individual provider and systems level, and advocate for and support data collection, reporting, and tracking by race and ethnicity across the region and state. We propose that these efforts, which are underway in most states, be extended to collecting data regarding ethnicity in clinical trial participation.

Recommendation 3—E*stablish Community-wide Disparities Work Groups*. Support the development and institutionalization of a special community council/partnership to 1) assist in the building of a community infrastructure to recruit, retain, and grow an academic, professional, and provider community, 2) establish a directory of minority health care providers, and 3) convene and co-sponsor community partnerships involving minority health providers, elected officials, professional associations, and local business community and other community stakeholders.

The Endocrine Society is in a strong position to encourage its clinician members to both take part in clinical trials and encourage their patients to volunteer for them. Furthermore, the Society can nurture interactions among its clinical scientists and its physicians in practice to encourage education on the needs of clinical research. Although the Society has its strengths, it alone cannot address the community or industry concerns with diversification. Therefore, in addition to the improvements recommended for federal agencies and pharmaceutical companies, **we endorse the creation and funding of a long-term and sustainable health disparities movement that is multicultural, multi-issue, and based on a set of broad social determinants of health, including education, employment, and housing.**

References Cited in Text

1. Parangimalil GJ. Latino health in the new millennium: The need for a culture-centered approach. Sociological Spectrum, 2001;21:423-9.
2. Gibbs BK, Prothrow-Stith D, Outreach to African-American communities: from theory to practice, in Ivor Livingston, ed. Handbook of Black American health: Policies and issues behind disparities in health (2 vol.; second ed.) Westport, Conn.: Greenwood Publishing Group; 2004. p. 667-81.
3. Smedley BD, Syme SL. Promoting health. Intervention strategies from social and behavioral research. Institute of Medicine. Washington, DC: National Academy Press; 2000.
4. Prothrow-Stith D, Gibbs BK, Allen A. Reducing health disparities: From theory to practice. Cancer Epidemiol Biomarkers Prev. 2003;12:256s-260s.

Additional References

Abraham M. Transforming marital violence from a "private problem" to a "public issue." South Asian Women's Organizations and Community Empowerment; 1995.

Boston Public Health Commission. Data report: A presentation and analysis of disparities in Boston, the disparities project; 2005.

Braithwaite RL, Taylor SE, editors. Health Issues in the black community. 2nd ed. San Francisco: Jossey-Bass; 2001. p.3-12; 62-80; 471-88; 543-59.

Brownson RC, Baker EA, Novick LF, editors. Community-based prevention: Programs that work. New York: Aspen Publishers; 1999. p. 169-70; 183-98.

Bullard RD. Dumping in Dixie: Race, class, and environmental quality. Boulder, Colo.: Westview Press; 1990. p. 33-5.

Bullard RD, editor. Confronting Environmental Racism: Voices from the grassroots. Boston: South End Press; 1993. p. 15-75.

Bullard RD, editor. Unequal protection: Environmental justice and communities of color. San Francisco: Sierra Club; 1994. p. 11-7; 234-43.

Bullard RD, Warren RC, Johnson GS. The quest for environmental justice. In: Braithwaite RL, Taylor S, editors. Health issues in the black community. 2nd ed. San Francisco: Jossey-Bass; 2001.

Byrd WM, Clayton LA. An American health dilemma, 2 vols. New York: Routledge; 2000-2001.

Gibbs BK, Nsiah-Jefferson L, McHugh M, Trivedi A, Prothrow-Stith D. Reducing racial and ethnic health disparities: Exploring an outcome oriented agenda for research and policy. Journal of Health Politics, Policy and Law. 2006 Mar;31(1):185-218.

Hacker A. Two nations: Black, white, separate, hostile, unequal. New York: Maxwell Macmillan; 1992.

Hofrichter R, editor. Toxic struggles: The theory and practice of environmental justice. Philadelphia: New Society Publishers; 1993.

Israel BA, Schulz AJ, Parker EA, Becker AB. Review of community-based research: Assessing partnership approaches to improve public health. Annu Rev Public Health. 1998;19:173–202.

Jones CP. The racism in "race." Presented at the annual meeting of the American Public Health Association, 1977.

Jones CP. Invited commentary: "Race," racism, and the practice of epidemiology. Am J Epidemiol. 2001;154:299-302.

Kawachi I, Kennedy BP, Lochner K, Prothrow-Stith D. Social capital, income inequality, and mortality. Am J Public Health. 1997;87:1491-8.

Kennedy BP, Kawachi I, Glass R, Prothrow-Stith D. Income distribution, socioeconomic status, and self-rated health: A U.S. multi-level analysis. BMJ. 1998;317:917-21.

Kennedy BP, Kawachi I, Prothrow-Stith D, Gupta V. Income inequality, social capital and firearm-related violent crime. Soc Sci Med. 1998;47:7-17.

Kennedy BP, Kawachi I, Lochner K, Jones C, Prothrow-Stith D. (Dis)Respect and black mortality. Am J Public Health. 1997;87:1491-8.

Lawson E, Young A. Health care revival renews, rekindles, and revives. Am J Public Health. 2002;92:177-9.

Mauss AL. Social problems as social movements. Philadelphia: Lippincott; 1975.

McDonough JE, Gibbs BK, Scott-Harris JL, et al. A state policy agenda to eliminate racial and ethnic health disparities. The Commonwealth Fund; June 2004.

Morris AD. The origins of the civil rights movement: Black communities organizing for change. New York: The Free Press; 1984. p. 277-90.

National Cancer Institute. Breast: U.S. racial/ethnic patterns. Available at http://www.cancer.gov/statistics/cancertype/breast-racial-ethnic.

National Center for Health Statistics. Infant, neonatal, and post neonatal mortality rates by race and sex: United States, 1975-2000. National Vital Statistics Report. 2002;50(15).

Office of Research and Health Statistics. Neighborhood health status report: The health of Roxbury. Division of Public Health, Trustees of Health and Hospitals Incorporated, the City of Boston; 1994.

Staples L. (1984). Roots to power: A manual for grassroots organizing. Westport, Conn: Praeger Publishers; 1984. p. 15-30.

Stith CR. Political religion. A liberal answer the question, "should politics and religion mix?" Nashville: Abingdon; 1995.

Stout L. Bridging the class divide and other lessons for grassroots organizing. Boston: Beacon Press; 1996. p. 117-40.

Taylor SE, Braithwaite RL. African American health. In: Braithwaite RL, Taylor SE, editors. Health issues in the black community. 2nd ed. San Francisco: Jossey-Bass; 2001.

Thomas SB, Quinn SC. Eliminating health disparities. In: Braithwaite RL, Taylor SE, editors. Health issues in the black community. 2nd ed. San Francisco: Jossey-Bass; 2001.

Trivedi, A., Gibbs, B., Nsiah-Jefferson, L., Ayanian, J., Prothrow-Stith, P., An evaluation of states capacity to address racial and ethnic health disparities: Creating a state minority health report card. Health Affairs. 2005 Mar/Apr;24:388-96.

Williams DR, Rucker TD. Understanding and addressing racial disparities in health care. Health Care Financ Rev. 2000;21:75-90.

Wilson WJ. When work disappears: The world of the new urban poor. New York: Knopf, Random House; 1996.

The Endocrine Society's Recommendations for Increasing Minority Involvement in Clinical Research

Recommendations for all stakeholders

- We recommend a consensus conference be held by NIH, or another appropriate agency, that comprises representatives from all stakeholder groups including, but not limited to, the NIH, the FDA, pharmaceutical companies/CROs, academic institutions, health-management organizations, community health networks, and community leaders, to discuss and form a plan to address the following issues:
  - **It is critical to undertake a collaborative effort by NIH, the pharmaceutical industry, and academic institutions** to expand the mandate of current programs to include resources for the development of a nationwide network of minority physician researchers and patient volunteers. We envision a national consortium sponsored by NIH (with support from the pharmaceutical industry) and hosted by academic institutions across the country. This consortium would provide training, mentoring, startup funds, and opportunities to participate in ongoing trials. Examples of alterations to existing mechanisms already funded by NIH that could lead to achieving these goals include, but are not limited to:

    1) Centers of Excellence in cancer, diabetes, and cardiovascular disease research could be supplemented to support community outreach programs that recruit and train diverse community-based practices.

    2) Supplements could be provided to support collaboration between these Centers of Excellence and historically black medical institutions.

    3) Granting mechanisms that support meeting requests by the Agency for Healthcare Research and Quality could be used to train minority researchers in good clinical research practices.

    4) Clinical fellowship training programs could carry supplements to support interactions between physician scientists based at academic institutions and physicians practicing in community centers.

    5) Small Business Innovation Research grants could be provided to expand the number of contract research organizations that recruit and train physicians from diverse sites.
  - The definitions in the Office of Management and Budget (OMB) Directive No. 15 (currently used by the NIH and the FDA) should be reviewed and revised to provide guidance on more appropriate and relevant ethnicity categorization so that information gathered will be scientifically sound and easily compared across federal agencies and from study to study.
  - Agreement must be reached on satisfactory parameters that provide for appropriate minority representation in a study. Parameters of inclusion might reasonably consist of current or projected population demographics, based on the epidemiology of the disease of interest. Parameters of inclusion should take into account disproportionate representation of disease in a given population and the number of patients from each affected subpopulation required to generate statistically significant data. Additional considerations might include the patent life of the drug in the context of projected demographics.
  - We need to consider the potential value of funding meta-analyses of existing safety and efficacy data for race and sex.

Recommendations for Congress

We encourage Congress to take the following steps in the order indicated:

- Establish and/or empower an Office of Minority Health within the Office of the FDA Commissioner, with a monitoring authority analogous to the Office of Women's Health established in 1994 to oversee changes suggested for the FDA (see below).
- Pass legislation requiring clinical trials to include women and minorities for FDA approval of drugs, similar to legislation passed in 1993 requiring the inclusion of these groups in NIH-funded trials.
- Provide incentives such as tax breaks or patent extensions for companies that adhere to FDA guidances on inclusion of minorities in clinical trials and/or

undertake additional trials. This mechanism has been used successfully to help companies undertake studies in pediatric populations.

Recommendations for FDA

- Establishing the validity of safety and efficacy data for women and minorities as appropriate should be a requirement for the approval of new drug applications and investigative new drug applications.
  - The FDA should consider immediate adoption of NIH guidelines on the inclusion of women and minority populations, as outlined in the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research, most recently amended in October 2001.
  - The FDA should then require rather than recommend adherence to its own guidelines. This requirement should be phased in over a period of time sufficient for CROs and pharmaceutical companies to build and access the resources needed to comply. During the transition, incentives such as those described above should be applied to companies meeting inclusion requirements.
  - The FDA should analyze data on minority participation comparing participation rates for phases I through IV clinical trials. This analysis should include past studies to the extent possible and future studies based on parameters determined at the consensus conference. A complete analysis that includes the number of patients invited to participate, the number of patients failing the screen, the number consenting, the number enrolled, and the number retained would be helpful to future planning efforts.

Recommendations for NIH (as funding agency) and academic institutions (as implementer)

- Adopt mechanisms such as the Department of Defense Small Business Innovation Research program that would encourage entrepreneurs to establish CROs and/or limited liability corporations (LLCs) dedicated to recruiting diverse physicians and study populations.
- Establish and maintain the infrastructure required for minority practitioners to participate in research studies sponsored by pharmaceutical agencies and universities. Specifically, it is important to have a registry of minority community practices from which individual investigators and researchers at academic institutions, CROs, and pharmaceutical companies could easily and efficiently recruit volunteers.
- Establish mentorship programs between academic institutions and community-based practices that are interested and willing to perform clinical research or to refer their patients to clinical trials. The mentoring can be for providers who want to learn good clinical research practices or those who want to facilitate their patients joining the trials. As an example, Baylor, Harvard, and Washington University in St. Louis are building such a research consortium and are maintaining such a registry of patients.
- Create and fund Community Research Advisory Boards at appropriate sites. These would be mandated to promote community-based participatory research by 1) facilitating communication between investigators and patients on the impediments to research participation at that site, 2) providing communication and feedback among the various stakeholders, 3) providing community oversight so that participants feel safe, and 4) allowing the community and its leaders to become positive process participants.
- Increase the pipeline by developing programs at medical schools aimed at increasing the enrollment and matriculation of diverse medical students as appropriate for the projected population changes over the next 30 years.
- Medical schools should offer training in good clinical research practice and cultural competencies to all trainees and staff members who may directly or peripherally engage in clinical research.

Appendix I

Personal Experience of Rhonda Bentley-Lewis, M.B.A., M.D.

Dr. Bentley-Lewis has participated in clinical research on several levels, from research coordinator to principal investigator, and has faced challenges at all of these levels. The following is her informal summary of some of her experiences.

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Distrust of "the system" of clinical research is a powerful deterrent to participation in clinical research by underrepresented minorities, particularly African Americans, given this country's history. As a research coordinator, although we were not targeting minority populations, I faced challenges from potential African American volunteers who were suspicious of clinical research. One volunteer directly questioned my motives and expressed concern that I would "say anything" to secure her study participation. She believed and expressed (in other words) that I knew the study was harmful but, because my allegiance was to the study and not to her individually, I was charged to solicit her participation. I know that this questioning and these concerns resulted from a deep level of distrust.

Beyond distrust, another factor limiting participation is physical access to the studies. If one does learn of a research study, transportation to the location may pose a challenge, due either to distance or to the unavailability of public transportation from the person's home. In addition, some of these populations are served largely by community centers not active in clinical research; consequently, these patients do not learn of the research opportunities.

Another significant barrier is the amount of remuneration. I have been limited (as are most researchers in academic settings, I believe) by the IRB in what I can offer volunteers in return for research participation. I appreciate that this is a valid restriction based on concerns about coercion. However, I have heard from several of my potential volunteers that the amount I offer in return for their research participation does not allow them to recover child care expenses or wages lost during that day. (Obtaining child care and taking time from work are additional challenges for some.) I realize that one cannot provide differential remuneration based on ethnicity or an expressed individual financial need; however, in my studies I reimburse for reasonable transportation expenses and try to work around work schedules. I have also considered the question of child care and whether the child can accompany the volunteer to the visit. Usually, this is an impractical option.

What are some possible solutions? I have developed specific activities targeted at the recruitment of African Americans. I have given presentations at churches and other African American community groups on diabetes prevention and management. During my presentation, I have not actually discussed my studies, but I have made flyers available on display tables. I'm not sure if discussing the study would dilute my message but I didn't want to confuse my intention to educate the group on good health practices with a "sales pitch." I also intend to post flyers in barbershops and Laundromats. Although I've mailed some flyers, I need to find time to get there personally because I think that will have a greater impact. I continue to seek out new resources and community alliances to facilitate my recruitment efforts.

Appendix II

Summary of Impediments and Best Practices: ENDO 06 Program Information

Academic Researcher: Neer
Pharmaceutical Researcher: No
NIH-funded: Yes
Disease/Condition Studied: Menopause
Grantor: NIH
Populations Sought: Black, African American, or Caribbean; Latina; Japanese or Japanese American; Chinese or Chinese American; self-described as white

Type of Community Involvement: Local medical practices, minority community leaders, and politicians

Perceived Recruitment Problems: Local demographics not conducive to diverse study population, community practitioners suspicious of losing patients to academic research centers, lack of community trust for research and researchers, incomplete voting lists prevented effective sampling by this method, unlisted telephone numbers prevented effective sampling by this method, religious and cultural difficulties.

Solutions: Used minority PR firm to design radio, billboard, and shopping center advertising in minority neighborhoods, used community television, recruited research assistants who were people of color, forged community coalitions.

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Academic Researcher: Auchus
Pharmaceutical Researcher: No
NIH-funded: No, foundation funded
Disease/Condition Studied: Coronary heart disease; biological differences among blacks, Hispanics, and whites emerged as an issue due to appropriate study design and successful recruitment efforts.

Grantor: Donald W. Reynolds Foundation

Populations Sought: Caucasian, African Americans

Type of Community Involvement: Civic and religious leaders, an in-house ethics committee, a community advisory board led to successful collaboration between the academic center and the community.

Perceived Recruitment Problems: Lack of health knowledge (untreated diabetes and misperceptions about hypertension), difficulty recruiting African American men.

Solutions: Inventive procedures for community-based interventions (medical students into local barbershops, etc.), worked closely with a community advisory board.

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Academic Researcher: Gibbs
Pharmaceutical Researcher: No
NIH-funded: Yes
Disease/Condition Studied: Reduce cardiovascular disease and other chronic health conditions in African Americans, eliminate disparities in minority health care.
Grantor: NIH
Minority Populations Sought: African American community
Type of Community Involvement: Community-Based Participatory Research (CBPR)
Perceived Recruitment Problems: Lack of knowledge about clinical research, lack of health insurance, fear and lack of trust for research and researchers, language and literacy, and time constraints in the African American community.

Solutions: Community-based approach to engaging the community to practice self-determination with respect to their health care needs, to create real incentives, and to allay fears.

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Academic Researcher: Thaler
Pharmaceutical Researcher: No
NIH-funded: N/A
Disease/Condition Studied: Patient education/awareness
Grantor: N/A; non-profit organization
Minority Populations Sought: Diverse populations
Type of Community Involvement: This non-profit organization educates public, patients, medical/research communities, media, and policy makers about clinical research participation.

Perceived Recruitment Problems: Lack of pre-education leads to clinical trial dropout rate of 25%, distrust in research/ers by the minority and general community, a preponderance of Caucasian research investigators leading to less participation by diverse volunteers, groups

most under-represented in clinical research are those least likely to have access to the internet—only 45% of African Americans and 38% of people with disabilities.

Solutions: Education awareness days, community partnerships, brochures, and local advertising.

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Academic Researcher: Ramsey
Pharmaceutical Researcher: Ramsey
NIH-funded: Some studies
Disease/Condition Studied: HIV/AIDS
Grantors: NIH and pharmaceutical companies
Minority Populations Sought: Persons with HIV/AIDS; minorities, particularly African American women.
Type of community Involvement: N/A

Perceived Recruitment problems: Despite being in a diverse area of Boston, it is difficult to get patients who can't afford the drug after the trial ends.

Solutions: Expanded access policy that provides the drug to volunteers who can't afford to purchase it after the trial ends.

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Academic Researcher: No
Pharmaceutical Researcher: Judith Johnson/pharmacovigilance for Genzyme and previous experience in CROs
NIH-funded: N/A
Disease/Condition Studied: Safety review of all Genzyme drugs
Grantor: Corporate funding, FDA regulated
Minority Populations Sought: African Americans, Latinos, Asian Americans
Type of Community Involvement: Education of health care providers
Perceived Recruitment Problems: Difficulty in recruiting sites run by minority physicians who are trained to do clinical research and sites run by minority or majority physicians in urban areas with diverse patients.

Solutions: Training new sites, targeting patient education and recruitment programs to the communities surrounding these sites.

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Academic Researcher: Moses (previously at Harvard)
Pharmaceutical Researcher: Moses (currently at Novo Nordisk, Inc.)
NIH-funded: N/A
Disease/Condition Studied: Diabetes
Grantor: Corporate funding, FDA regulated
Minority Populations Sought: African Americans, Latinos, Asian Americans
Type of Community Involvement: Fund education of health care providers
Perceived Recruitment Problems: European companies have difficulty recruiting minority patients to their early studies.

Solutions: Identifying and training new sites in diverse areas.

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Summary Notes
Stephanie B. Kutler, Associate Director, Government & Professional Affairs, The Endocrine Society

Two over-arching trends in the information

1) There is a great distrust of researchers (and clinical research) by minority groups and referring physicians.
    a. Referring physicians (of all races) fear that they will lose their patients if they [their patients] enroll in a clinical trial.
    b. Majority of researchers are Caucasian.
    c. Not enough involvement of the community as a conduit to the minority groups by researchers.

2) Lack of education about clinical research and its benefits:
    a. Referring physicians are not aware of the trials.
    b. Incomplete voting lists and a high % of unlisted numbers.
    c. One of the main sources of information on clinical trials is the Internet, and a high percentage of minority groups do not have access to it.
    d. Participants feel more like guinea pigs than someone doing something good for the community, particularly when access to the drug ends with the trial.
    e. Not enough pre-education to help potential participants understand the process and the benefits of the research.

The Endocrine Society's Task Force on Increasing Minority Participation in Clinical Research

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American Association of Endocrine Surgeons
American Diabetes Association
American Society for Reproductive Medicine
American Society of Andrology
American Thyroid Association
Androgen Excess Society
Lawson Wilkins Pediatric Endocrine Society
Pediatric Endocrinology Nursing Society
Society for Gynecologic Investigation
Society for the Study of Reproduction
The American Society for Bone and Mineral Research
The Hormone Foundation
The Obesity Society

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